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=> s her2 or (her(w)2) or erbB2 or cerbB2 or ((erb or cerb)(w)b2) or ((erbB or
cerbB)(w)2) or p158?
L8       42801 HER2 OR (HER(W) 2) OR ERBB2 OR CERBB2 OR ((ERB OR CERB)(W) B2)
               OR ((ERBB OR CERBB)(W) 2) OR P158?

=> s anti(2w)l8
L9        3018 ANTI(2W) L8

=> s l8(3a)antibod?
L10       4109 L8(3A) ANTIBOD?

=> s l9 or l10
L11       4946 L9 OR L10

=> s l11 and py<1992
   2 FILES SEARCHED...
L12        150 L11 AND PY<1992

=> dup rem l12
PROCESSING COMPLETED FOR L12
L13         67 DUP REM L12 (83 DUPLICATES REMOVED)
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Phase II study of weekly intravenous trastuzumab (Herceptin) in patients with HER2/neu-overexpressing metastatic breast cancer.

Baselga J, Tripathy D, Mendelsohn J, Baughman S, Benz CC, Dantis L, Sklarin NT, Seidman AD, Hudis CA, Moore J, Rosen PP, Twaddell T, Henderson IC, Norton L.

Semin Oncol. 1999 Aug;26(4 Suppl 12):78-83.

Department of Medicine, Services of Breast and Gynecological Cancer Medicine and Clinical Immunology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA.

The HER2/neu proto-oncogene is overexpressed in 25% to 30% of patients with breast cancer. Trastuzumab (Herceptin; Genentech, San Francisco, CA), a recombinant humanized monoclonal antibody with high affinity for the HER2 protein, inhibits the growth of breast cancer cells overexpressing HER2. In this phase II study the efficacy and toxicity of weekly administration of trastuzumab was evaluated in 46 patients with metastatic breast cancer whose tumors overexpressed HER2. A loading dose of 250 mg trastuzumab was administered intravenously, which was followed by 10 weekly doses of 100 mg each. Upon completion of this treatment period, patients with no disease progression could receive a weekly maintenance dose of 100 mg. Patients in this trial had extensive metastatic disease, and most had received prior anticancer therapy. Ninety percent of patients achieved adequate serum levels of trastuzumab. Toxicity was minimal, and no antibodies against trastuzumab could be detected. Objective responses were observed in 5 of the 43 evaluable patients, which included 1 complete remission and 4 partial remissions, for an overall response rate of 11.6%. Responses were seen in mediastinum, lymph nodes, liver, and chest wall lesions. Minor responses (seen in 2 patients) and stable disease (14 patients) lasted for a median of 5.1 months. These results demonstrate that trastuzumab is well tolerated and clinically

active in patients with HER2-overexpressing metastatic breast cancers who have received extensive prior therapy. The regression of human cancer through the targeting of putative growth factor receptors such as HER2 warrants further evaluation of trastuzumab in the treatment of breast cancer.

Publication Types:
- Clinical Trial
- Clinical Trial, Phase Ii
- Journal Article

MeSH Terms:
- Adult
- Antibodies, Monoclonal/pharmacokinetics/*therapeutic use
- Antineoplastic Agents/pharmacokinetics/*therapeutic use
- Breast Neoplasms/*drug therapy/metabolism/pathology
- Female
- Human
- Middle Aged
- Neoplasm Metastasis
- Receptor, erbB-2/*immunology
- Support, Non-U.S. Gov't
- Support, U.S. Gov't, P.H.S.

Substances:
- 0 (Antibodies, Monoclonal)
- 0 (Antineoplastic Agents)
- 0 (trastuzumab)
- EC 2.7.1.112 (Receptor, erbB-2)

Grant Support:
- P50-CA58207/CA/NCI

PMID: 10482197 [PubMed - indexed for MEDLINE]

From PubMed

L4 ANSWER 1 OF 1 MEDLINE
ACCESSION NUMBER: 95316868 MEDLINE
DOCUMENT NUMBER: 95316868 PubMed ID: 7796420
TITLE: Topological control of p21WAF1/CIP1 expression in normal and neoplastic tissues.
AUTHOR: el-Deiry W S; Tokino T; Waldman T; Oliner J D; Velculescu V
E; Burrell M; Hill D E; Healy E; Rees J L; Hamilton S R; +
CORPORATE SOURCE: Oncology Center, Johns Hopkins University School of Medicine, Baltimore, Maryland 21231, USA.
CONTRACT NUMBER: CA43460 (NCI)
CA62924 (NCI)
GM07184 (NIGMS)
SOURCE: CANCER RESEARCH, **(1995 Jul 1) 55** (13) **2910-9.**
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U24170; GENBANK-U24171; GENBANK-U24172; GENBANK-U24173; GENBANK-U24174
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950817
Last Updated on STN: 19950817
Entered Medline: 19950801

AB The p53-regulated gene product p21WAF1/CIP1 is the prototype of a family of small proteins that negatively regulate the cell cycle. To learn more about p21WAF1/CIP1 regulation in vivo, monoclonal antibodies were developed for immunohistochemistry. These revealed that p21WAF1/CIP1 expression followed radiation-induced DNA damage in human skin in a pattern consistent with its regulation by p53. A detailed comparison of the human, rat, and mouse p21WAF1/CIP1 promoter sequences revealed that this induction was probably mediated by conserved p53-binding sites upstream of the transcription start site. In unirradiated tissues, p21WAF1/CIP1 expression was apparently independent of p53 and was observed in a variety of cell types. Moreover, there was a striking compartmentalization of p21WAF1/CIP1 expression throughout the gastrointestinal tract that correlated with proliferation rather than differentiation. As epithelial cells migrated up the crypts, the Ki67-expressing proliferating compartment near the crypt base ended abruptly, with the coincident appearance of a nonproliferating compartment expressing p21WAF1/CIP1. In colonic neoplasms, this distinct compartmentalization was largely abrogated. Cell cycle inhibitors are thus subject to precise topological control, and escape from this regulation may be a critical feature of neoplastic transformation.

L1 ANSWER 1 OF 1 MEDLINE on STN
ACCESSION NUMBER: 96313760 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8694549
TITLE: Apoptosis and angiogenesis: two promising tumor markers in breast cancer (review).
AUTHOR: Wu J
CORPORATE SOURCE: Academic Department of Biochemistry, Royal Marsden Hospital, London, U.K.
SOURCE: Anticancer research, **(1996 Jul-Aug) 16** (4B) **2233-9**. Ref: 80
Journal code: 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199608
ENTRY DATE: Entered STN: 19960911
Last Updated on STN: 19960911
Entered Medline: 19960829

AB Mammary epithelial homeostasis is dependent not only on the rate of cell proliferation, but also on apoptosis, a genetically programmed process of autonomous cell death. Cell death in tumours is commonly attributed to the induction of apoptosis. Angiogenesis is the process leading to the formation of new blood vessels, and it has been proposed that tumor growth is angiogenesis dependent. This review focuses on the biological role of apoptosis and angiogenesis in the development and progression of breast cancer; on the multiple genetic pathways regulating apoptosis and angiogenesis in breast cancer; and on clinical data demonstrating the prognostic significance of apoptosis and angiogenesis in breast cancer. Although evidence has suggested that decreased apoptosis and increased angiogenesis may play important roles in the biological aggressiveness of breast cancer, their precise molecular mechanisms in mammary tumorigenesis are unknown. There is accumulating evidence that apoptotic pathways and angiogenic status are controlled by a number of regulators, including inducers and inhibitors relevant to the pathogenesis of breast cancer. The inhibition of angiogenesis limits tumor growth by elevating the incidence of apoptosis. Several clinical studies have shown that apoptosis and angiogenesis are novel prognostic indicators in breast cancer, and they may have predictive value for the response to anticancer treatments. A recent study suggested that increased apoptosis plays a role in the response to hormonal treatment of breast cancer. Other studies have indicated that patients with breast cancer with high angiogenic activity have a worse prognosis. Overall, the evidence suggests that the progressive inhibition of apoptosis and induction of angiogenesis may contribute to tumor initiation, growth and metastasis in the pathogenesis of breast cancer. Apoptosis and angiogenesis may be valuable as markers for response in patients having primary or adjuvant chemotherapy for breast cancer. Furthermore, such tumor markers have the potential to develop a promising therapeutic strategy to regulate cell survival/death and neovascularization in breast cancer by the induction of apoptosis and/or the inhibition of angiogenesis.

L3 ANSWER 1 OF 1 MEDLINE on STN
ACCESSION NUMBER: 1999285173 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10356685
TITLE: Update on the management of advanced breast cancer.
AUTHOR: **Fornier M**; Munster P; Seidman A D
CORPORATE SOURCE: Breast Cancer Medicine Service, Memorial Sloan-Kettering Cancer Center, New York, New York, USA.
SOURCE: Oncology (Williston Park, N.Y.), **(1999 May) 13** (5) **647-58; discussion 660, 663-4.**
Ref: 88
Journal code: 8712059. ISSN: 0890-9091.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990715
Last Updated on STN: 19990715
Entered Medline: 19990708

AB Recent trials comparing single-agent vs combination therapy in metastatic breast cancer suggest that it may be time to reconsider the belief that combination chemotherapy is the gold standard of treatment. Based on the limited randomized trial data available to date, high-dose chemotherapy with stem-cell rescue should not be viewed as "state-of-the art" treatment for metastatic disease and should be used only in the context of clinical trials. Recent trials have explored the optimal dosing and scheduling of the taxanes, as well as the possible role of these agents in combination regimens. Capecitabine (Xeloda), a new oral fluoropyrimidine, appears to be comparable in efficacy to CMF (cyclophosphamide, methotrexate, and fluorouracil), and preclinical data suggest possible synergy between this agent and the taxanes. Other promising agents under study include liposome-encapsulated doxorubicin (TLCD-99), an immunoconjugate linking a chimeric human/mouse monoclonal antibody to doxorubicin molecules; MTA (LY231514), a multitargeted antifolate; and marimistat, a broad-spectrum matrix metalloproteinase inhibitor. Tamoxifen (Nolvadex) remains the most important hormonal agent, but new antiestrogens and selective estrogen receptor modulators (SERMs) may provide alternatives. The potential role of new aromatase inhibitors as first-line hormonal agents requires further study. Finally, the possible synergy between trastuzumab (Herceptin), a recombinant humanized monoclonal antibody to the HER-2/neu protein, and paclitaxel (Taxol) is being studied in two clinical trials.

L6 ANSWER 1 OF 1 MEDLINE on STN
ACCESSION NUMBER: 92277689 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1317462
TITLE: Accumulation of p53 tumor suppressor gene protein: an independent marker of prognosis in breast cancers.
AUTHOR: Thor A D; Moore DH I I; Edgerton S M; Kawasaki E S; Reihsaus E; Lynch H T; Marcus J N; Schwartz L; Chen L C; Mayall B H; +
CORPORATE SOURCE: Department of Pathology, Massachusetts General Hospital, Boston 02114.
CONTRACT NUMBER: CA-44768 (NCI)
CA-48802 (NCI)
SOURCE: Journal of the National Cancer Institute, **(1992 Jun 3) 84** (11) **845-55.**
Journal code: 7503089. ISSN: 0027-8874.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 19920710
Last Updated on STN: 19920710
Entered Medline: 19920626

AB BACKGROUND: Mutations of the tumor suppressor gene p53 have been identified in breast cancer cell lines, and some breast carcinomas are detectable by immunohistochemical assay because of p53 protein accumulation. PURPOSE: This study was designed to determine whether p53 protein accumulation in breast cancers correlates with p53 gene mutation, with survival, and with five pathobiologic factors associated with prognosis. METHODS: IgG1 monoclonal antibody to human p53 protein (PAb 1801) and immunohistochemical methods were used to detect p53 protein accumulation in archival formalin-fixed, paraffin-embedded, randomly selected carcinomas. We studied 295 invasive ductal carcinomas from the Massachusetts General Hospital; 151 were determined to be sporadic (not hereditary). We also studied 97 invasive ductal carcinomas--21 sporadic and 76 familial (hereditary)--from Creighton University. In addition, we examined 31 archival in situ carcinomas, 15 snap-frozen invasive ductal carcinomas, primary cell cultures from three benign breast tissue samples, and breast carcinoma cell lines MDA-MB-231 and MDA-MB-468. RESULTS: Nuclear p53 protein was observed in 16% of the 31 in situ carcinomas, 22% of the 172 sporadic carcinomas, 34% of the 50 tumors from patients with familial breast cancer, 52% of the 23 tumors from patients with the familial breast and ovarian cancer syndrome, and all three tumors from two patients with the Li-Fraumeni syndrome. There was complete concordance between p53 gene mutation and p53 protein accumulation in the 15 snap-frozen carcinomas and in both breast carcinoma cell lines. Statistically significant associations of p53 protein accumulation with estrogen receptor negativity and with high nuclear grade were found. There were statistically significant associations, independent of other prognostic factors, between p53 protein accumulation and metastasis-free and overall survival, for randomly accrued and for both sporadic and familial tumors. CONCLUSIONS: Immunohistochemically detected p53 protein accumulation was an independent marker of shortened survival and was seen more often in familial than in sporadic carcinomas. Our findings also suggest a correlation between p53 protein accumulation and p53 gene mutation.